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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE  
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NATIONAL INSTITUTES OF HEALTH  
BETHESDA, MARYLAND 20014

September 1, 1977

Dr. Joshua Lederberg  
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Stanford, California 94305

Dear Dr. Lederberg:

Thank you for your letter of August 10, which informs us that you plan to submit an application for the February 1, 1978 deadline. There is, of course, and as you recognize, some risk to you in this later submission, since review would only be completed some seven months prior to the lapse of the current project period. In the case of an adverse review, this could result in some loss of continuity of funding, since there would not be enough time to compete for alternate sources of funds. Nevertheless, I do agree that the advantage of submitting a superior application may well outweigh that risk.

I also agree that you may qualify for a Genetics Research Center. To this end, I am enclosing a separate covering letter which we are now sending to center grant applicants, along with some draft versions of instructions on the preparation of center grant applications. I am also enclosing the "General Guidelines for NIGMS Center Grants" and "NIGMS Genetic Centers: Intention, Prerequisites, and Guidelines". Note particularly that we consider it extremely important that we review a draft application well in advance of formal submission to the Division of Research Grants.

I would like to make an additional point since I was struck by the phrase in your letter that your group "might be able to qualify for recognition as a Genetics Research Center" (underlining is mine). Although I realize that the designation of NIGMS Genetics Center has, in the minds of some, been felt to be a mark of special recognition for excellence, we ourselves have never really felt that way about them. Rather, we think of them as an appropriate response to a special set of circumstances which include a marked amount of collaboration among the center participants, and one or a few scientific foci and common themes. Furthermore, we would wish to see both clinical and "model-systems oriented" research represented and some evidence of potential for cross-fertilization. Finally, the separate projects must be of a quality that would make them competitive with research projects reviewed individually by study sections.

Any group of investigators that can meet these criteria is eligible to apply for a center. Note that some of the better U.S. genetics groups have never applied for a center. Other applicants have failed as centers, even though the specific individuals applying were, in the opinions of the reviewers,

outstanding. The circumstances, however, were such that individual awards made more sense than one large Genetics Center award. In summary, a center grant is not a "prestige" award; it is merely a mechanism of funding a group of people which makes good sense to our reviewers, and to our Institute.

Let me discuss some other aspects of your letter:

The Primary Responsibilities of the Principal Investigator for Program Leadership: Let me start with a quote from one of the documents I sent you:

"Since several departments, both basic and clinical, generally will be involved, there must be a center director of sufficient stature to be a recognized and effective leader, supported by an appropriate administrative structure, appointed and given the responsibility and appropriate authority to administer the program. The administrative structure needs to be clearly delineated. The director may operate with advice of a scientific advisory committee but responsibility of the program by a committee is not desirable."

Let me enlarge on that statement: The funding of such centers implies flexibility in shifting ideas, experiments, and funds as some projects decrease in relative significance in relation to others (possibly this can even include new and presently unanticipated projects within the scope and mission of the Center, and the funds available.) Leadership in implementing such use of funds for maximum effectiveness is expected of the Center Director. He may rely on the advice of a committee, but the final responsibility for performance is his.

In other words, I feel that the Center Director is not fulfilling his function if he acts solely as a disbursing agent for predetermined sets of funds. I therefore agree to the comment in your letter that funds allocated for specific projects are "understood to be points of departure, rather than firm commitments of resource allocation throughout the life of the grant." However, let me also emphasize that this sort of flexibility is one of degree: One person's flexibility may be another's flaccidity. Although rebudgeting between projects, and initiation or termination of some efforts is implicit in the center grant mechanism, it is also important that very marked changes of direction or effort between reviews be done with the understanding and consent of Institute staff. This, of course, implies a better-than-average exchange of information. Proposals or plans for very marked deviations should, I feel, require interim administrative review.

The premise that the program project or center should be directed to core support for shared, interdisciplinary and innovative activities, leaving to the submission of individual research proposals those efforts that have reached the point of maturity, so they can be effectively reviewed that way: As you know, I did have some problems with understanding precisely what you had in mind here, and thus called you up. I gather that you are saying that

there are some ongoing projects that are funded under other auspices, and that will not be included in the application. There are some new projects which, you feel, can be very competitive and receive favorable review. These will require some shared core facilities which will also be requested. All this seems reasonable. The important thing here is that the reviewers and the Institute get a feel of the degree of commitment of every one concerned to the aims of the program-project or center, as compared to other research obligations. To this end, the table of "other support" and the time/effort figures are often examined and discussed by the reviewers.

I think another thing to keep in mind is that the "Center" as an intellectual environment and focus for related investigations may be far larger than the "Center" as a funding instrument. Some applications therefore include a descriptive section on related activities, by center participants and their associates, for which no funds are requested by which may contribute to the overall environment.

The Current Status and Authorization of the Genetics Center Efforts. Is this a Credible Objective to Aspire to? The answer is yes. In the past year, a number of the Genetics Centers which started some four years ago had their first re-review. Some did not survive, either because of the quality of the individual projects, or because of problems with leadership or cohesion. Unfortunately, we have noted that this has engendered some rumors that NIGMS "was getting out of the Centers business". We are not, and, in fact, most of the clinical research in Genetics and a lot of model-systems oriented research of our program continues to be supported by the Genetics Centers. However, we do insist that there be no compromise with quality in comparison to research funded by the individual project grants.

I am pleased that you plan to be in close touch with us as your plans proceed, and look forward to hearing from you.

Sincerely yours,



Fred H. Bergmann, Ph.D.  
Program Director, Genetics  
National Institute of  
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Enclosures: Letter to Lederberg, 8/29/77 (draft instructions)  
General Guidelines, NIGMS Research Center Grants  
NIGMS Genetics Centers: Intention, Prerequisites & Guidelines